The dyskerin ribonucleoprotein complex as an OCT4/SOX2 coactivator in embryonic stem cells.

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Public Summary:
Acquisition of pluripotency is driven largely at the transcriptional level by activators OCT4, SOX2, and NANOG that must in turn cooperate with diverse coactivators to execute stem cell-specific gene expression programs. Using a biochemically defined in vitro transcription system, we report the purification and identification of the dyskerin (DKC1) ribonucleoprotein complex as one such OCT4/SOX2 coactivator. The DKC1 complex occupies enhancers and regulates the expression of key pluripotency genes critical for self-renewal in embryonic stem (ES) cells. Depletion of DKC1 in fibroblasts significantly decreased the efficiency of induced pluripotent stem (iPS) cell generation. This study thus reveals an unanticipated transcriptional role of the DKC1 complex in stem cell maintenance and somatic cell reprogramming.

Scientific Abstract:
Acquisition of pluripotency is driven largely at the transcriptional level by activators OCT4, SOX2, and NANOG that must in turn cooperate with diverse coactivators to execute stem cell-specific gene expression programs. Using a biochemically defined in vitro transcription system that mediates OCT4/SOX2 and coactivator-dependent transcription of the Nanog gene, we report the purification and identification of the dyskerin (DKC1) ribonucleoprotein complex as an OCT4/SOX2 coactivator whose activity appears to be modulated by a subset of associated small nucleolar RNAs (snoRNAs). The DKC1 complex occupies enhancers and regulates the expression of key pluripotency genes critical for self-renewal in embryonic stem (ES) cells. Depletion of DKC1 in fibroblasts significantly decreased the efficiency of induced pluripotent stem (iPS) cell generation. This study thus reveals an unanticipated transcriptional role of the DKC1 complex in stem cell maintenance and somatic cell reprogramming.